

REMARKS

The Office Action of August 18, 2008, has been received and reviewed. The claims are to be amended are previously set forth. New claims 19-36 are presented herein. Basis for new claims 19-36 can be found throughout the Specification as filed and more specifically at Table 1, and original claims 10-18. All amendments are made without prejudice or disclaimer. No new matter has been presented. Reconsideration is respectfully requested.

Interview

Applicants' representative would like to thank the Examiner for the courtesy extended him during the telephonic interview of July 31, 2008 to request an election of species. During that interview applicants elected 1) heptyl-D-alpha-mannopyranoside, wherein R0 = O and R1 = n-pentyl, 2) *Escherichia coli*, and 3) urinary tract infection. Applicants hereby affirm that election in response to the outstanding Office Action. If the Office believes that further comments are necessary or desired describing the interview, the Examiner is kindly requested to contact applicants' undersigned attorney, and further detail will be promptly provided.

Rejections under 35 U.S.C. § 103(a)

Claims 10-14 stand rejected under 35 U.S.C. § 103(a) as assertedly being obvious over Nagahori *et al.* (Chem. BioChem. (2002) vol. 3, p. 836-844) (hereinafter "Nagahori") in view of Choudhury *et al.* (Science, vol. 285, P. 1061-1066) (hereinafter "Choudhury") and Bouckaert (Glycoconjugate J., vol. 18, p. 31) (hereinafter "Bouckaert") (collectively hereinafter "the references"). Applicants respectfully traverse the rejections as hereinafter set forth.

To establish a *prima facie* case of obviousness, the prior art itself or "the inferences and creative steps that a person of ordinary skill in the art would [have] employ[ed]" at the time of the invention are to have taught or suggested the claim elements. Additionally, the Examiner must determine whether there is "an apparent reason to combine the known elements in the fashion claimed by the patent at issue." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740-1741, 167 L.Ed.2d 705, 75 USLW 4289, 82 U.S.P.Q.2d 1385 (2007). Further, rejections on obviousness grounds "cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of

obviousness.” *Id* at 1741, quoting *In re Kahn*, 441, F.3d 977, 988 (Fed. Cir. 2006). “Often, it will be necessary for a [fact finder] to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed To facilitate review, this analysis should be made explicit.” *Id*. Furthermore, to establish a *prima facie* case of obviousness there must have been a reasonable expectation of success. M.P.E.P. § 2143.02. Underlying the obvious determination is the fact that statutorily prohibited hindsight cannot be used. *KSR*, 127 S.Ct. at 1742.

Applicants respectfully submit that the references cannot make obvious the elected species of n-pentyl as neither the prior art itself nor the inferences and creative steps that a person of ordinary skill in the art would have employed at the time of the invention teach or suggest the elected species of n-pentyl. The Examiner asserts that Nagahori suggests the use of a long aliphatic chain or an aromatic ring immediately next to the mannose sugar to produce the best inhibitors. Office Action at page 7. However, Nagahori does not indicate how long a “long” aliphatic chain should be and does not indicate that an n-pentyl chain would be so considered.

Applicants respectfully submit that holding n-pentyl obvious would amount to an “obvious to try” standard. In relation to “obvious to try,” the courts have recently noted that “[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp.” *KSR International Co. v. Teleflex Inc. et al.*, *supra*, at 17. Applicants respectfully submit that the references provide no finite number of identified, predictable solutions to the problem generating binding inhibitors for the pilus of a gram-negative bacterium.

Except for those very limited circumstances outlined in *KSR*, “obvious to try” has consistently been held not to be the standard for obviousness under 35 U.S.C. § 103. *See, e.g.*, *In re Goodwin*, 576 F.2d 375, 377, 198 USPQ 1, 3 (CCPA 1978); *In re Tomlinson*, 363 F.2d 938, 150 USPQ 623 (CCPA 1966). The Federal Circuit has held that:

The admonition that “obvious to try” is not the standard under § 103 has been directed . . . [to cases where] what would have been “obvious to try” would have been to vary all parameters or to try each of numerous possible choices until one

possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. *In re O'Farrell*, 853 F.2d at 903.

This is precisely the case in regard to the instant claims. In the Office Action, it was asserted that the use of a long aliphatic chain ... immediately next to the mannose sugar to produce the best inhibitors. Office Action at page 7. Applicants disagree with the notion that the references specifically suggest or teach the use of n-pentyl as such a long aliphatic chain. Nagahori, at most, suggests the use of any "long aliphatic chain or aromatic ring immediately next to the mannose sugar." Nagahori at p. 836, col. 1, paragraph 2. Thus, Nagahori suggests millions of possible compounds in one sentence.

The references provide no disclosure as to the various types and/or kinds of long aliphatic chains or aromatics rings this encompasses, or the effects, advantages, and/or disadvantages resulting therefrom. One would have to try each of the numerous possible choices, until a long aliphatic chain or aromatic ring that actually displayed good binding to a pilus was arrived at. Further, the references give no direction, other than "long aliphatic chains or aromatics rings," as to which possible C1 additions are likely to be successful. In addition, n-pentyl, n-hexyl, n-heptyl, and n-octyl are never specifically mentioned or suggested, other than as part of a massive group, for use in the creation of possible molecules capable of binding the gram-negative pilus. Therefore, although it might have been "obvious to try" every possible combination of all known long aliphatic chains and aromatic rings, this would not render the elected n-pentyl group obvious under the meaning of 35 U.S.C. § 103.

In re O'Farrell held that the claims therein were obvious because the prior art contained detailed enabling methodology for practicing the claimed invention, a suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful. *In re O'Farrell*, 853 F.2d at 902. In the present case, the references may indicate that it is possible to create the D-alpha-mannose with the n-pentyl group, though not specifically and with over a million other possible aliphatic chains or aromatic groups in one sentence. As such, the situation present *In re O'Farrell* is factually distinguishable from the present case, and for the reasons outlined therein and discussed above, the present claims are not made obvious by the references under 35 U.S.C. § 103(a).

In addition, applicants respectfully submit that the low K_d value for n-pentyl is an

unexpected result. The D-alpha-mannose with the n-pentyl group shows binding two orders of magnitude stronger than mannose or D-alpha-mannose with an n-methyl group. In addition, the D-alpha-mannose with the n-pentyl group shows binding one order of magnitude stronger than mannose or D-alpha-mannose with an n-propyl or n-ethyl group. Applicants respectfully submit that one of ordinary skill in the art would have found that greatly increased binding of the D-alpha-mannose with the n-pentyl group to be an unexpected result given the large change in binding affinity.

The Examiner notes that the dissociation constants presented in Table 1 do not indicate their standard deviations or statistical significance. Office Action at page 9. In the IDS accompanying this response, applicants supply the paper of Bouckaert *et al.* in which Table 1 of the current application is published as Table 1 at page 443. Applicants note that the statistical significance of these numbers is inherent in the fact that they were accepted and published by a peer reviewed journal. Further, the statistical significance of the related dissociation constants is made plain by the fact that the differences in the change in the constant are two orders of magnitude (as noted above). Notwithstanding, applicants herewith provide the declaration of Julie Bouckaert in which the standard deviations of the K_d values are presented in the column labeled SD K_d . As can be seen therein, the K_d value for the n-pentyl mannose is indeed statistically significant over the n-methyl through n-butyl D-alpha-mannoses.

Applicants would also like to point out that where $R_0 = CH_2$, and given the ethyl between R_0 and R_1 , that in order to arrive at the linear pentyl-, hexyl-, heptyl-, and octyl alpha-D-mannosides currently claimed, that R_1 is then ethyl, propyl, butyl, or pentyl, and that where R_0 is O or S, and given the ethyl between R_0 and R_1 , that R_1 is then propyl, butyl, pentyl, or hexyl.

In view of at least the foregoing, applicants respectfully request withdrawal of the rejections of claims 10-14 under 35 U.S.C. §103(a) and reconsideration of same.

Rejoinder

Applicants respectfully request rejoinder of claims 15-18, 24-27, and 33-35 as claims 10, 19, and 28 are generic for these claims. Further, if claims require all the limitations of an allowable claim, those claims will be eligible for rejoinder. M.P.E.P. § 821.04; *see also In re Ochiai*, 71 F.3d 1565 (Fed. Cir. 1995); *In re Brouwer*, 77 F.3d 422 (Fed. Cir. 1996). Applicants

respectfully submit that each of claims 15-18 and 24-27 incorporate all of the limitations of one of claims 10 or 19. Applicants believe claims 10 and 19 are in condition for allowance. As such, applicants respectfully request the rejoinder of claims 15-18 and 24-27 which each include all the elements of one of allowable claims 10 and 19.

CONCLUSION

In light of the above amendments and remarks, applicants respectfully request reconsideration of the application. If questions remain after consideration of the foregoing, or if the Office should determine that there are additional issues which might be resolved by a telephone conference, the Office is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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Enclosures: IDS
Declaration of Julie Bouckaert